

Received March 9, 2021, accepted March 25, 2021, date of publication April 5, 2021, date of current version April 13, 2021.

Digital Object Identifier 10.1109/ACCESS.2021.3071038

# Optimal Experimental Design for Uncertain Systems Based on Coupled Differential Equations

YOUNGJOON HONG<sup>1,2</sup>, BONGSUK KWON<sup>3</sup>, AND  
BYUNG-JUN YOON<sup>4,5</sup>, (Senior Member, IEEE)

<sup>1</sup>Department of Mathematics and Statistics, San Diego State University, San Diego, CA 92182, USA

<sup>2</sup>Department of Mathematics, Sungkyunkwan University, Suwon 440-746, Republic of Korea

<sup>3</sup>Department of Mathematical Sciences, Ulsan National Institute of Science and Technology, Ulsan 44919, Republic of Korea

<sup>4</sup>Department of Electrical and Computer Engineering, Texas A&M University, College Station, TX 77843, USA

<sup>5</sup>Brookhaven National Laboratory, Upton, NY 11973, USA

Corresponding author: Byung-Jun Yoon (bjyoon@ece.tamu.edu)

The work of Youngjoon Hong was supported by the Collaboration Grant for Mathematicians, Simons Foundation. The work of Bongsuk Kwon was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) by the Ministry of Science, ICT and Future Planning under Grant NRF-2020R1A2C1A01009184. The work of Byung-Jun Yoon was supported in part by the National Science Foundation (NSF) under Award 1835690 and in part by the Department of Energy (DOE) under Award DE-SC0019303.

**ABSTRACT** We consider the optimal experimental design (OED) problem for an uncertain system described by coupled ordinary differential equations (ODEs), whose parameters are not completely known. The primary objective of this work is to develop a general experimental design strategy that is applicable to any ODE-based model in the presence of uncertainty. For this purpose, we focus on non-homogeneous Kuramoto models in this study as a vehicle to develop the OED strategy. A Kuramoto model consists of  $N$  interacting oscillators described by coupled ODEs, and they have been widely studied in various domains to investigate the synchronization phenomena in biological and chemical oscillators. Here we assume that the pairwise coupling strengths between the oscillators are non-uniform and unknown. This gives rise to an uncertainty class of possible Kuramoto models, which includes the true unknown model. Given an uncertainty class of Kuramoto models, we focus on the problem of achieving robust synchronization of the uncertain model through external control. Should experimental budget be available for performing experiments to reduce model uncertainty, an important practical question is how the experiments can be prioritized so that one can select the sequence of experiments within the budget that can most effectively reduce the uncertainty. In this paper, we present an OED strategy that quantifies the objective uncertainty of the model via the mean objective cost of uncertainty (MOCU), based on which we identify the optimal experiment that is expected to maximally reduce the MOCU. We demonstrate the importance of quantifying the operational impact of the potential experiments in designing optimal experiments and show that the MOCU-based OED scheme enables us to minimize the cost of robust control of the uncertain Kuramoto model with the fewest experiments compared to other alternatives. The proposed scheme is fairly general and can be applied to any uncertain complex system represented by coupled ODEs.

**INDEX TERMS** Mean objective cost of uncertainty (MOCU), optimal experimental design (OED), objective uncertainty quantification (objective UQ), Kuramoto model.

## I. INTRODUCTION

In many real-world applications, we often have to deal with complex systems, for which we do not have complete knowledge. While collecting more data may lead to better system

modeling, there exist many scientific applications in which gathering sufficient data for accurate system identification is practically impossible due to the enormous complexity of the system, prohibitively high cost of data acquisition, or both. Relevant examples abound across various domains, including multi-scale climate modeling for long-term prediction, inference of genome-scale regulatory network for predicting

The associate editor coordinating the review of this manuscript and approving it for publication was Grigore Stamatescu.

effective intervention strategies, characterization of a material system for optimization of targeted functional properties, just to name a few. In such cases, experimental design should target improving one's knowledge of the uncertain system on aspects that critically affect one's operational goals, which may be related to control, classification, filtering, or others.

In this paper, we consider the problem of optimal experimental design (OED) for an uncertain complex system based on coupled ordinary differential equations (ODEs). Specifically, we focus on the Kuramoto oscillator model [1], [2] as a vehicle to develop the OED capabilities, which could be ultimately applied to any uncertain model based on coupled ODEs beyond the Kuramoto model. The Kuramoto model has been widely studied by many researchers and has a rich published literature. However, the model has not been much investigated for cases when there is substantial uncertainty in the model.

The primary goal of this paper is to identify the optimal experiment that is expected to effectively reduce the model uncertainty in such a way that minimizes the cost of controlling the uncertain system. The mean objective cost of uncertainty (MOCU) [3] can be used to quantify the objective-based uncertainty, which then can be used to predict the optimal experiment that maximally reduces the uncertainty pertaining the cost of control [4]. Recently, MOCU-based OED has been applied to a number of applications such as gene regulatory network intervention [4], [5], adaptive sequential sampling [6], active learning [7], [8], robust filtering [9], and autonomous materials discovery [10]. While the Kuramoto model has been extensively studied in the past, we would like to note that neither the objective-based uncertainty quantification (UQ) of uncertain Kuramoto models nor OED strategies for reducing the uncertainty present therein have been studied to date. For the first time, we tackle the experimental design problem for an uncertain coupled-ODE system. Unlike previous studies [4]–[6], [9]–[12], we do not assume experiments can directly measure the unknown parameters. Instead, we consider realistic experiments, whose outcomes may be used to narrow down the range of the unknown parameters rather than exactly estimating them, which may not be always possible in real applications.

## II. UNCERTAIN KURAMOTO MODEL

### A. KURAMOTO MODEL OF INTERACTING OSCILLATORS

We consider the Kuramoto model:

$$\dot{\theta}_i(t) = \omega_i + \sum_{j=1}^N a_{i,j} \sin(\theta_j(t) - \theta_i(t)), \quad i = 1, \dots, N, \quad (1)$$

where  $\theta_i = \theta_i(t)$  is the phase of the  $i$ -th oscillator with the intrinsic natural frequency  $\omega_i$ ,  $a_{i,j}(= a_{j,i})$  represents the coupling strength constant between the  $i$ -th and the  $j$ -th oscillators, and  $N$  is the total number of oscillators in the model. The system (1) was first introduced by Yoshiki Kuramoto in [1], [2] to describe the phenomena

of collective synchronization observed in the systems of chemical and biological oscillators, in which an ensemble of oscillators spontaneously locks to a common frequency, despite the differences in the natural frequencies of the individual oscillators. This model makes assumptions that (i) the oscillators are all-to-all, weakly coupled and that (ii) the pairwise interaction between two oscillators depends sinusoidally on their phase difference. From a mathematical point of view, the model can be derived by employing the normal form calculation and perturbation method for a system of globally coupled differential equations with stable limits cycles, which is discussed in great details in [2]. Such collective synchronization phenomena have been observed and investigated in various domains, where circadian rhythms [13], cortical oscillations in neuroscience [14], [15], and synchronously flashing fireflies [16] are well-known examples in biology. There are also examples in engineering and physics, for instance, arrays of lasers [17] and superconducting Josephson junction arrays [18]. There have been extensive studies for the Kuramoto model shown in (1), and we refer interested readers to [19], [20] for excellent reviews addressing the motivation, derivation, and applications of the model. We also refer to [21]–[23] and the references therein for other recent theoretical developments.

It is worth noting that the analysis of Kuramoto models in the past, especially their synchronization phenomena, has been made based on mean-field coupling [11], [12]. Although analytic solutions exist for conditions that guarantee the synchronization of Kuramoto models, they only apply to special cases, such as the homogeneous case when all pairwise coupling strength parameters  $a_{i,j}$  are uniform. In our work, we do not constrain our model to such cases, and  $a_{i,j}$  can take arbitrary values that are different for different oscillator pairs  $(i, j)$ . For example, we may even have  $a_{i,j} = 0$  for some pairs  $(i, j)$ , such that the interaction graph underlying the Kuramoto model may not be fully connected.

### B. UNCERTAINTY CLASS OF KURAMOTO MODELS

For Kuramoto models, it is known that the underlying network structure is closely related to synchronization, yet the precise relation is not well understood. Especially we consider the situation where the coupling strengths in the network (1) are not fully known.

More precisely, we consider a set of  $N$  Kuramoto oscillators, where the natural frequency  $\omega_i$  is known for all oscillators. However the interaction strength  $a_{i,j}$  between the  $i$ -th and the  $j$ -th oscillators is not known with certainty. Instead, we assume that only a lower bound  $a_{i,j}^l$  and an upper bound  $a_{i,j}^u$  is known for  $a_{i,j}$ . This gives rise to an uncertainty class  $\mathcal{A}$  of  $N$  interacting Kuramoto oscillators, where  $\mathbf{a} = \{a_{i,j}\}$ ,  $1 \leq i < j \leq N$  is an uncertain parameter vector. We assume that  $\mathbf{a}$  is uniformly distributed in  $\mathcal{A}$  following the prior distribution below:

$$p(\mathbf{a}) = \begin{cases} c, & \text{if } a_{i,j} \in [a_{i,j}^l, a_{i,j}^u], \quad \forall i, j \\ 0, & \text{otherwise} \end{cases} \quad (2)$$

where

$$c = \prod_{i=1}^{N-1} \prod_{j=i+1}^N \frac{1}{(a_{i,j}^u - a_{i,j}^l)}. \quad (3)$$

### C. QUANTIFYING THE OBJECTIVE COST OF UNCERTAINTY

When this uncertain Kuramoto model is initially non-synchronous, can we bring it to synchronization via external control, for example, by connecting an additional oscillator to the rest of the oscillators to catalyze the synchronization? If so, how can it be done optimally? Suppose we want to ensure the frequency synchronization of the  $N$  interacting Kuramoto oscillators with uncertain interaction strength  $\mathbf{a} \in \mathcal{A}$  by adding an additional oscillator which interacts with the  $N$  oscillators in the original system. Here the Kuramoto oscillator ensemble  $\vartheta(t) := (\theta_1(t), \dots, \theta_N(t))$  is said to achieve *the frequency synchronization asymptotically* if it locks to a common frequency such that

$$\lim_{t \rightarrow \infty} |\dot{\theta}_i(t) - \dot{\theta}_j(t)| = 0 \quad \text{for all } 1 \leq i, j \leq N. \quad (4)$$

We assume that the  $(N + 1)$ -th oscillator added to the original system for control (*i.e.*, to achieve frequency synchronization) has a known natural frequency  $\omega_{N+1}$  and that its interaction strength with the  $i$ -th oscillator (part of the original system) is uniform  $a_{i,N+1} = a_{N+1}$ ,  $\forall i = 1, \dots, N$ . By selecting a sufficiently large interaction strength  $a_{N+1}$ , we can enforce all  $N$  oscillators in the original system to be synchronized with each other in terms of their oscillation frequency (*i.e.*, angular speed). With the introduction of the additional oscillator, now we have

$$\begin{aligned} \dot{\theta}_i(t) = \omega_i + \sum_{j=1}^N a_{i,j} \sin(\theta_j(t) - \theta_i(t)) \\ + a_{N+1} \sin(\theta_{N+1}(t) - \theta_i(t)) \end{aligned} \quad (5)$$

for  $i = 1, \dots, N$ . Although  $a_{N+1} \rightarrow \infty$  would guarantee synchronization, our goal is to minimize the interaction strength  $a_{N+1}$  as it affects the cost of control, a larger  $a_{N+1}$  resulting in a higher cost for synchronizing the oscillators in the system.

For a given  $\mathbf{a}$ , we define  $\xi(\mathbf{a})$  as the minimum value of the interaction strength  $a_{N+1}$  that guarantees synchronization of all oscillators. As  $a_{N+1} = \xi(\mathbf{a})$  would be optimal for a specific  $\mathbf{a}$ , we call it  $\xi(\mathbf{a})$  the *optimal interaction strength*. In the presence of uncertainty, we are unable to identify  $\xi(\mathbf{a})$  since  $\mathbf{a}$  is unknown. Instead, we desire an *optimal robust interaction strength*  $\xi^*(\mathcal{A})$  such that

$$\xi^*(\mathcal{A}) = \max_{\mathbf{a} \in \mathcal{A}} \xi(\mathbf{a}). \quad (6)$$

Note that it is robust because  $a_{N+1} = \xi^*(\mathcal{A})$  guarantees synchronization for any  $\mathbf{a} \in \mathcal{A}$ . It is optimal because it is the smallest such value. As we can see from (6),  $a_{N+1}$  increases due to the uncertainty, which forces us to choose a larger interaction strength than might be actually needed for synchronization. The expected increase of this differential

cost can be measured by computing the expected value of the cost increase

$$M(\mathcal{A}) = \mathbb{E}_{\mathbf{a}} [\xi^*(\mathcal{A}) - \xi(\mathbf{a})], \quad (7)$$

based on  $p(\mathbf{a})$ , which governs the distribution of  $\mathbf{a}$  within the uncertainty class  $\mathcal{A}$ . This average differential cost  $M(\mathcal{A})$  is referred to as the *mean objective cost of uncertainty (MOCU)* [3], and it quantifies the impact that the model uncertainty has on the operational objective. When there are two or more objectives, the definition of MOCU in (7) can be further extended as shown in [24].

### III. OPTIMAL EXPERIMENTAL DESIGN

Suppose we want to perform additional experiments to reduce the uncertainty class. In general, the outcome of an experiment may reduce the uncertainty class, which may help us predict a better robust controller—in this case, the  $(N + 1)$ -th oscillator with a smaller interaction strength  $a_{N+1} = \xi^*(\mathcal{A})$  that ensures the synchronization of all oscillators despite the uncertainty in  $\mathbf{a}$ . While the original oscillators do not necessarily have to be non-synchronous, in such a case the cost of controlling (synchronizing) the Kuramoto model would be zero. To avoid such trivial cases, we assume in our examples that the oscillators in the original model are non-synchronous. A practical question arises naturally: among the possible experiments, how can we select the optimal experiment? We address this question in what follows.

#### A. EXPERIMENTAL DESIGN SPACE

We restrict our experimental design space to experiments that test pairwise synchronization between oscillators. Suppose we choose the oscillator pair  $(i, j)$  for our experiment, where we initialize the angles to  $\theta_i(0) = \theta_j(0)$  and observe whether the two oscillators will become eventually synchronized in the absence of any influence from all other oscillators. We define a binary random variable  $B_{i,j}$  for the experimental outcome, where  $B_{i,j} = 1$  corresponds to the eventual synchronization of the oscillator pair, while  $B_{i,j} = 0$  corresponds to the opposite.

If the interaction strength  $a_{i,j}$  between the oscillators  $i$  and  $j$  were known, the outcome  $B_{i,j}$  would be known with certainty. In fact, Theorem 1 below shows that the oscillator pair will be synchronized if and only if  $|\omega_i - \omega_j| \leq K$ , where  $K = 2a_{i,j}$  in this case.

*Theorem 1: Consider the Kuramoto model of two-oscillators:*

$$\begin{aligned} \dot{\theta}_1(t) &= \omega_1 + \frac{K}{2} \sin(\theta_2(t) - \theta_1(t)), \\ \dot{\theta}_2(t) &= \omega_2 + \frac{K}{2} \sin(\theta_1(t) - \theta_2(t)) \end{aligned} \quad (8)$$

with the initial angles  $\theta_1(0), \theta_2(0) \in [0, 2\pi)$ . Then, for any solutions  $\theta_1$  and  $\theta_2$  to (8), there holds  $|\dot{\theta}_1(t) - \dot{\theta}_2(t)| \rightarrow 0$  as  $t \rightarrow \infty$  if and only if  $|\omega_1 - \omega_2| \leq K$ .

*Proof:* First assume that  $|\omega_1 - \omega_2| \leq K$ . By symmetry, we may assume without loss of generality, that  $\omega_1 \geq \omega_2$  and

that  $\theta_1(0) - \theta_2(0) \in [0, 2\pi)$ . By subtracting the equations of (8), one has

$$\dot{\Theta}(t) = \omega_1 - \omega_2 - K \sin(\Theta(t)) =: F(\Theta(t)), \quad (9)$$

where  $\Theta(t) := \theta_1(t) - \theta_2(t)$ . Since  $0 \leq \omega_1 - \omega_2 \leq K$ , there is a number  $\Theta_* \in [0, \pi/2]$  such that  $\sin \Theta_* = (\omega_1 - \omega_2)/K \in [0, 1]$ . We can easily check that  $F'(\Theta_*) = -K \cos \Theta_* \leq 0$ , indicating that  $\Theta_*$  is a unique (mod  $2\pi$ ) stable critical point of (9). This implies that  $\Theta(t) \rightarrow \Theta_* \pmod{2\pi}$  as  $t \rightarrow \infty$  unless  $\Theta(0) = \pi - \Theta_*$ , in turn  $\dot{\Theta}(t) \rightarrow 0$ . When  $\Theta(0) = \pi - \Theta_*$ , which is an unstable critical point, we have  $\Theta(t) = \pi - \Theta_*$  for all  $t \geq 0$ . These prove our assertion. On the other hand, if  $|\omega_1 - \omega_2| > K$ , one has from (9) that

$$\begin{aligned} |\dot{\theta}_1(t) - \dot{\theta}_2(t)| &\geq |\omega_1 - \omega_2| - K |\sin(\theta_1(t) - \theta_2(t))| \\ &\geq |\omega_1 - \omega_2| - K \\ &> 0. \end{aligned} \quad (10)$$

This completes the proof.  $\square$

However, the uncertainty regarding  $a_{i,j}$  renders  $B_{i,j}$  a random variable whose outcome is unknown before performing the pairwise synchronization experiment described above. Suppose our experiment results in the eventual synchronization of the two oscillators ( $B_{i,j} = 1$ ). Based on Theorem 1, the inequality  $|\omega_i - \omega_j| \leq 2a_{i,j}$  must hold. This experimental outcome allows us to update the lower bound of  $a_{i,j}$  from  $a_{i,j}^\ell$  to  $\tilde{a}_{i,j}^\ell$  defined as

$$\tilde{a}_{i,j}^\ell = \max\left(\frac{1}{2}|\omega_i - \omega_j|, a_{i,j}^\ell\right). \quad (11)$$

On the other hand, we have  $|\omega_i - \omega_j| > 2a_{i,j}$  if the oscillators do not get synchronized ( $B_{i,j} = 0$ ), which allows us to update the upper bound of  $a_{i,j}$  from  $a_{i,j}^u$  to  $\tilde{a}_{i,j}^u$  given by

$$\tilde{a}_{i,j}^u = \min\left(\frac{1}{2}|\omega_i - \omega_j|, a_{i,j}^u\right). \quad (12)$$

In either case, the pairwise experiment can potentially reduce the uncertainty regarding  $a_{i,j}$ , thereby shrinking the uncertainty class  $\mathcal{A}$ .

## B. SELECTING THE OPTIMAL EXPERIMENT

Knowing that the aforementioned pairwise experiments can potentially reduce the uncertainty class, how should we prioritize the experiments to select the optimal one? The MOCU framework can be used to predict the optimal experiment that is expected to maximally reduce the uncertainty [4]–[6], [9] in such a way that minimizes the cost of uncertainty, namely, the expected cost increase for controlling (*i.e.*, synchronizing) the  $N$  Kuramoto oscillators due to the uncertain interaction strength. More specifically, for every experiment in the experimental design space, we first compute the expected remaining MOCU after performing the given experiment. Based on these results, we can prioritize the experiments and select the one that is expected to minimize the MOCU that remains after carrying out the experiment.

For convenience, let us denote the uncertainty class  $\mathcal{A}$  reduced based on the experimental outcome  $B_{i,j}$  as  $\mathcal{A}|B_{i,j}$ .

Then the expected remaining MOCU for the synchronization experiment of the oscillator pair  $(i, j)$  can be computed by

$$\begin{aligned} R(i, j) &= \mathbb{E}_{B_{i,j}}[M(\mathcal{A}|B_{i,j})] \\ &= \sum_{b \in \{0,1\}} Pr(B_{i,j} = b) M(\mathcal{A}|B_{i,j} = b) \end{aligned} \quad (13)$$

Based on the prior  $p(\mathbf{a})$  in (2), we can compute the probabilities for the possible experimental outcomes as follows

$$Pr(B_{i,j} = 1) = \frac{a_{i,j}^u - \tilde{a}_{i,j}}{a_{i,j}^u - a_{i,j}^\ell}, \quad (14)$$

$$Pr(B_{i,j} = 0) = \frac{\tilde{a}_{i,j} - a_{i,j}^\ell}{a_{i,j}^u - a_{i,j}^\ell} \quad (15)$$

where we define

$$\tilde{a}_{i,j} = \min\left(\max\left(\frac{1}{2}|\omega_i - \omega_j|, a_{i,j}^\ell\right), a_{i,j}^u\right) \quad (16)$$

to ensure that  $\tilde{a}_{i,j} \in [a_{i,j}^\ell, a_{i,j}^u]$ . The optimal oscillator pair, the outcome of whose pairwise synchronization experiment is expected to most effectively improve the control performance among the  $\binom{N}{2}$  pairs can be predicted by

$$(i^*, j^*) = \arg \min_{1 \leq i < j \leq N} R(i, j). \quad (17)$$

## C. COMPUTATIONAL COMPLEXITY

While computing the entropy of an uncertain coupling strength takes a fixed amount of time  $\mathcal{O}(1)$ , the computation of MOCU in (7) requires solving the ordinary differential equation in (1) multiple times to estimate the expectation based on Monte Carlo sampling. As a result, the computational complexity of computing the MOCU defined in (7) is

$$\mathcal{O}(TSN^2), \quad (18)$$

where  $T$ ,  $S$ , and  $N$  denote the final duration of time for solving the differential equation, the sample size (for Monte Carlo sampling), and the number of oscillators in the Kuramoto model, respectively. For practical values of these parameters, please see Section IV. However, we would like to note that the computation of MOCU does not take a large amount of time in practice, since the main MOCU computation module can be highly parallelized by taking advantage of modern GPU programming. In fact, we implemented our code using PyCUDA [25] and ran our simulations with Nvidia GTX 1080-Ti, which reduces the overall computational cost by  $\frac{1}{n}$ , where  $n = 57,344$  is the maximum number of CUDA cores in the graphic card. This massive parallelization allows us to reduce the computational cost significantly by increasing the number of threads on the thread block. For instance, the average runtime for the MOCU computation module was about 2.87 seconds when  $N = 5$ ,  $T = 4$ , and  $S = 20,000$ .



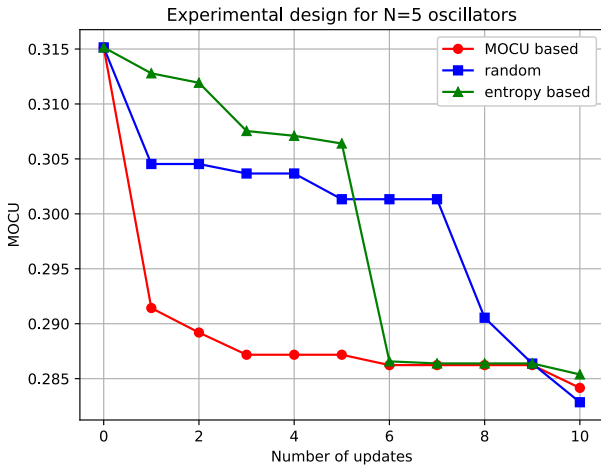
#### IV. SIMULATION RESULTS

In this section, we present numerical experiments to demonstrate our proposed OED method described in Section III-C. A classical fourth-order Runge-Kutta method is used to compute the Kuramoto model in (1) for  $0 \leq t \leq T$  for  $T = 5$  with time discretization  $\Delta t = 1/160$ . For the sake of simplicity, the initial conditions are set to  $\theta_i = 0$ ,  $1 \leq i \leq N$ . As the system is regular enough, the Runge-Kutta solvers provide reasonably accurate numerical solutions. For instance, the relative  $L^2$ -error of a five-oscillator model ( $N = 5$ ) is  $10^{-10} \sim 10^{-9}$  at  $t = T$ . Due to the immense uncertainty in parameters, the sample size  $S$  for computing the expectation in (7) should be sufficiently large (e.g.  $S \geq 20,000$ ) to obtain reliable experimental results. In this regard, massive computing power is highly desired, and we adopt GPU parallel computing, PyCUDA [25], using Nvidia GTX 1080-Ti.

As a paradigm example, we first implemented a 5-oscillator Kuramoto model. The following natural frequencies were used for the experiment in Figure 1:  $w_1 = -2.5000$ ,  $w_2 = -0.6667$ ,  $w_3 = 1.1667$ ,  $w_4 = 2.0000$ ,  $w_5 = 5.8333$ . For the additional oscillator used for control, we simply chose  $w_6 = \text{mean}_{1 \leq i \leq 5} w_i$ . The upper and lower bounds of interaction strength were chosen by

$$a_{i,j}^u = 1.15 d_{i,j} \left( \frac{1}{2} |w_i - w_j| \right),$$

$$a_{i,j}^l = 0.85 d_{i,j} \left( \frac{1}{2} |w_i - w_j| \right)$$



**FIGURE 1.** The model uncertainty decreases with sequential experimental updates. The MOCU-based scheme is clearly the most efficient, quickly reducing the uncertainty in fewer updates.

where  $d_{i,j}$  is a correction constant. If  $d_{i,j} \equiv 1$  for all  $i, j$ , the system is already synchronized in general as all entries of the interaction strength  $a_{i,j}$  are large enough. Hence, we introduced the correction parameter  $d_{i,j}$  such that

$$d_{i,j} = \begin{cases} 1, & (i, j) \in \mathcal{I}_1, \\ d_{i,j}^*, & (i, j) \in \mathcal{I}_2, \end{cases}$$

where  $0.3 \leq d_{i,j}^* \leq 0.5$ , and  $\mathcal{I}_1$  and  $\mathcal{I}_2$  are partition of the set of indices  $\mathcal{I} = \{(i, j) \in \mathbb{N} : 1 \leq i, j \leq N, i < j\}$ . Here, the set  $\mathcal{I}_1, \mathcal{I}_2$  and the corresponding quantity  $d_{i,j}^*$  were empirically determined. This results in a class of uncertain Kuramoto models that are non-synchronous, fully connected, but whose coupling strengths are uncertain.

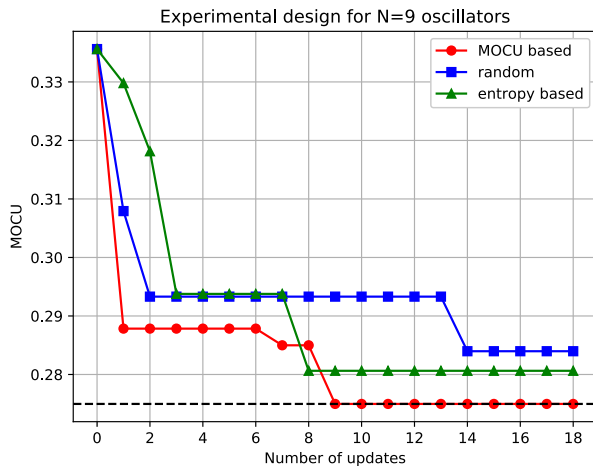
To compare numerical results, we carried out a sequence of experiments based on three different experiment selection strategies: MOCU-based, random selection, and entropy-based. In the MOCU-based selection strategy, the pairwise experiment with the smallest expected remaining MOCU in (13) was chosen, and the corresponding entry of  $a_{i,j}^u$  or  $a_{i,j}^l$  was updated based on the experimental outcome. More precisely, from the result of the pairwise experiment between the  $i$ -th and the  $j$ -th oscillators, if the oscillators were synchronized, then the lower bound  $a_{i,j}^l$  was updated to  $\tilde{a}_{i,j}$  defined in (16). Otherwise, the upper bound  $a_{i,j}^u$  was updated to  $\tilde{a}_{i,j}$ . In the entropy-based approach, we selected the pairwise experiment with the largest value of  $a_{i,j}^u - a_{i,j}^l$ , and the corresponding entry of  $a_{i,j}^u$  or  $a_{i,j}^l$  was updated based on the outcome in the same fashion. In the random approach, we randomly chose one of the  $\binom{N}{2}$  possible experiments and updated the corresponding entry of  $a_{i,j}^u$  or  $a_{i,j}^l$  based on the experimental outcome. Figure 1 shows that while all three methods eventually reached the minimum attainable uncertainty level after exhausting all experiments, the MOCU-based experiment selection strategy led to the most efficient updates. Especially, it identified effective experiments early on, nearly reaching the minimum attainable uncertainty level in just 3 updates.

Next, we conducted numerical simulations with a larger number of oscillators,  $N = 9$ , in which case the number of possible experiments increases to  $\binom{9}{2} = 36$ . We used the following natural frequencies:  $w_1 = 1.19$ ,  $w_2 = 3.23$ ,  $w_3 = 6.34$ ,  $w_4 = 7.48$ ,  $w_5 = 10.9$ ,  $w_6 = 11.62$ ,  $w_7 = 14.74$ ,  $w_8 = 29.58$ ,  $w_9 = 38.88$ . We set the natural frequency of the additional oscillator to  $w_{10} = \frac{1}{2} \text{mean}_{1 \leq i \leq 9} w_i$ . To start with a non-synchronized model, we selected sufficiently large natural frequencies for  $w_8$  and  $w_9$ . The upper and lower bounds of the interaction strengths were set to

$$a_{i,j}^u = 1.03 d_{i,j} \left( \frac{1}{2} |w_i - w_j| \right),$$

$$a_{i,j}^l = 0.97 d_{i,j} \left( \frac{1}{2} |w_i - w_j| \right)$$

where  $d_{i,j}$  is the correction parameter and that was empirically determined as in the previous example. Figure 2 shows the simulation results, which clearly demonstrate that the MOCU-based experimental design results in the most efficient updates among all three methods. Here we considered up to 18 updates (out of 36 experiments in total). As shown in Figure 2, the MOCU-based OED was able to drastically reduce uncertainty with a single update, and it reached the minimum uncertainty level just in 9 updates.



**FIGURE 2.** The model uncertainty decreases with sequential experimental updates. The baseline shows the minimum attainable uncertainty after all possible updates (36 experiments in total).

## V. CONCLUDING REMARKS

As shown in our results, designing effective experiments for complex uncertain systems requires quantifying the state of our current knowledge of the system and measuring the impact of the remaining uncertainty on the operator performance. It is clear that we cannot expect system-agnostic black-box optimization schemes to perform well.

Furthermore, experiments that aim to enhance our knowledge regarding parameters with the largest uncertainties do not necessarily help, as they may not be pertinent to the operator performance. Our work shows that the MOCU-based OED framework can effectively prioritize the experiments in the design space by quantifying the impact of their potential outcomes on the operational goal using scientific knowledge as in Theorem 1.

The proposed OED strategy can be immediately applied to various scientific problems that utilize Kuramoto models for studying synchronization phenomena in diverse fields. For example, Kuramoto models have been widely used for investigating brain network synchronization [26], [27] and its relation to neurological disorders [28]. Different brain regions may be represented by different oscillators in a Kuramoto model, where the coupling strengths reflect the underlying neuronal connectivity between regions. The resulting Kuramoto model is well-known for its capability to effectively capture oscillatory brain dynamics [26], [27]. The graph structure underlying the Kuramoto model and the actual coupling strength may not be known with certainty and they may have to be estimated from neuroimaging data [29], [30] or through experiments that combine imaging techniques with noninvasive brain stimulation [31]. The uncertain Kuramoto model may be used for various tasks, including the prediction of a personalized structure–function relationship [32] or therapeutic modulation of brain activity for management of neurological disorders [28], [31].

Beyond the Kuramoto models, on which we focused in this study, our MOCU-based OED strategy can be adapted

to a wide range of other uncertain systems that are described by ordinary differential equations. For example, one may apply the proposed OED scheme to the effective uncertainty reduction in non-linear systems considered in [33]–[35].

An interesting direction for future research is to expand the experimental design space to encompass experiments, whose outcomes cannot be directly used to measure the uncertain model parameters (as assumed in many past studies [4]–[6], [9], [10]) or to reduce model uncertainty by leveraging mathematical theorems (as we have proposed in this work). In general, we expect that taking a Bayesian approach would be most effective for addressing this inverse problem [36]–[38], and we are currently investigating strategies for Bayesian inversion of experimental outcomes to effectively reduce the objective model uncertainty.

## REFERENCES

- [1] Y. Kuramoto, “Self-entrainment of a population of coupled non-linear oscillators,” in *Proc. Int. Symp. Math. Problems Theor. Phys.* Berlin, Germany: Springer, 1975.
- [2] Y. Kuramoto, *Chemical Oscillations, Waves, and Turbulence*. Chelmsford, MA, USA: Courier Corporation, 2003.
- [3] B.-J. Yoon, X. Qian, and E. R. Dougherty, “Quantifying the objective cost of uncertainty in complex dynamical systems,” *IEEE Trans. Signal Process.*, vol. 61, no. 9, pp. 2256–2266, May 2013.
- [4] R. Dehghannasiri, B.-J. Yoon, and E. R. Dougherty, “Optimal experimental design for gene regulatory networks in the presence of uncertainty,” *IEEE/ACM Trans. Comput. Biol. Bioinf.*, vol. 12, no. 4, pp. 938–950, Jul. 2015.
- [5] R. Dehghannasiri, B.-J. Yoon, and E. R. Dougherty, “Efficient experimental design for uncertainty reduction in gene regulatory networks,” *BMC Bioinf.*, vol. 16, no. S13, pp. 1–18, Dec. 2015.
- [6] A. Broumand, M. S. Esfahani, B.-J. Yoon, and E. R. Dougherty, “Discrete optimal Bayesian classification with error-conditioned sequential sampling,” *Pattern Recognit.*, vol. 48, no. 11, pp. 3766–3782, Nov. 2015.
- [7] G. Zhao, E. Dougherty, B.-J. Yoon, F. Alexander, and X. Qian, “Uncertainty-aware active learning for optimal Bayesian classifier,” in *Proc. 9th Int. Conf. Learn. Represent. (ICLR)*, 2021, pp. 1–20.
- [8] G. Zhao, E. Dougherty, B.-J. Yoon, F. Alexander, and X. Qian, “Bayesian active learning by soft mean objective cost of uncertainty,” in *Proc. 24th Int. Conf. Artif. Intell. Statist. (AISTATS)*, 2021, pp. 3970–3978.
- [9] G. Zhao, X. Qian, B.-J. Yoon, F. J. Alexander, and E. R. Dougherty, “Model-based robust filtering and experimental design for stochastic differential equation systems,” *IEEE Trans. Signal Process.*, vol. 68, pp. 3849–3859, 2020.
- [10] A. Talapatra, S. Boluki, T. Duong, X. Qian, E. Dougherty, and R. Arróyave, “Autonomous efficient experiment design for materials discovery with Bayesian model averaging,” *Phys. Rev. Mater.*, vol. 2, no. 11, Nov. 2018, Art. no. 113803.
- [11] A. Arenas, A. Díaz-Guilera, J. Kurths, Y. Moreno, and C. Zhou, “Synchronization in complex networks,” *Phys. Rep.*, vol. 469, no. 3, pp. 93–153, Dec. 2008. [Online]. Available: <http://www.sciencedirect.com/science/article/pii/S0370157308003384>
- [12] H. Sakaguchi, “Cooperative phenomena in coupled oscillator systems under external fields,” *Prog. Theor. Phys.*, vol. 79, no. 1, pp. 39–46, Jan. 1988, doi: [10.1143/PTP.79.39](https://doi.org/10.1143/PTP.79.39).
- [13] C. Liu, D. R. Weaver, S. H. Strogatz, and S. M. Reppert, “Cellular construction of a circadian clock: Period determination in the suprachiasmatic nuclei,” *Cell*, vol. 91, no. 6, pp. 855–860, Dec. 1997.
- [14] M. Breakspear, S. Heitmann, and A. Daffertshofer, “Generative models of cortical oscillations: Neurobiological implications of the Kuramoto model,” *Frontiers Human Neurosci.*, vol. 4, p. 190, Nov. 2010. [Online]. Available: <https://www.frontiersin.org/article/10.3389/fnhum.2010.00190>
- [15] R. Schmidt, K. J. R. LaFleur, M. A. de Reus, L. H. van den Berg, and M. P. van den Heuvel, “Kuramoto model simulation of neural hubs and dynamic synchrony in the human cerebral connectome,” *BMC Neurosci.*, vol. 16, no. 1, p. 54, Dec. 2015, doi: [10.1186/s12868-015-0193-z](https://doi.org/10.1186/s12868-015-0193-z).

- [16] J. Buck and E. Buck, "Synchronous fireflies," *Sci. Amer.*, vol. 234, no. 5, pp. 74–79, 82, 1976. [Online]. Available: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-0016957851&partnerID=D=40&md5=8df5bc665b2604b1515357d881356393>
- [17] Z. Jiang and M. McCall, "Numerical simulation of a large number of coupled lasers," *J. Opt. Soc. Amer. B, Opt. Phys.*, vol. 10, no. 1, pp. 155–163, Jan. 1993. [Online]. Available: <http://josab.osa.org/abstract.cfm?URI=josab-10-1-155>
- [18] K. Wiesenfeld, P. Colet, and S. H. Strogatz, "Synchronization transitions in a disordered Josephson series array," *Phys. Rev. Lett.*, vol. 76, no. 3, pp. 404–407, Jan. 1996.
- [19] S. H. Strogatz, "From Kuramoto to Crawford: Exploring the onset of synchronization in populations of coupled oscillators," *Phys. D, Nonlinear Phenomena*, vol. 143, nos. 1–4, pp. 1–20, Sep. 2000.
- [20] J. A. Acebrón, L. L. Bonilla, C. J. Pérez Vicente, F. Ritort, and R. Spigler, "The Kuramoto model: A simple paradigm for synchronization phenomena," *Rev. Modern Phys.*, vol. 77, no. 1, pp. 137–185, Apr. 2005, doi: [10.1103/RevModPhys.77.137](https://doi.org/10.1103/RevModPhys.77.137).
- [21] F. Dörfler and F. Bullo, "On the critical coupling for Kuramoto oscillators," *SIAM J. Appl. Dyn. Syst.*, vol. 10, no. 3, pp. 1070–1099, Jan. 2011.
- [22] F. Dörfler and F. Bullo, "Synchronization and transient stability in power networks and nonuniform Kuramoto oscillators," *SIAM J. Control Optim.*, vol. 50, no. 3, pp. 1616–1642, Jan. 2012.
- [23] A. Gushchin, E. Mallada, and A. Tang, "Synchronization of heterogeneous Kuramoto oscillators with graphs of diameter two," in *Proc. 49th Annu. Conf. Inf. Sci. Syst. (CISS)*, Mar. 2015, pp. 1–6.
- [24] B.-J. Yoon, X. Qian, and E. R. Dougherty, "Quantifying the multi-objective cost of uncertainty," 2020, *arXiv:2010.04653*. [Online]. Available: <http://arxiv.org/abs/2010.04653>
- [25] A. Klöckner, N. Pinto, Y. Lee, B. Catanzaro, P. Ivanov, and A. Fasih, "PyCUDA and PyOpenCL: A scripting-based approach to GPU runtime code generation," *Parallel Comput.*, vol. 38, no. 3, pp. 157–174, Mar. 2012.
- [26] M. G. Kitzbichler, M. L. Smith, S. R. Christensen, and E. Bullmore, "Broadband criticality of human brain network synchronization," *PLoS Comput. Biol.*, vol. 5, no. 3, Mar. 2009, Art. no. e1000314.
- [27] H. Choi and S. Mihalas, "Synchronization dependent on spatial structures of a mesoscopic whole-brain network," *PLOS Comput. Biol.*, vol. 15, no. 4, Apr. 2019, Art. no. e1006978.
- [28] A. Mohseni, S. Gharibzadeh, and F. Bakouie, "The role of driver nodes in managing epileptic seizures: Application of Kuramoto model," *J. Theor. Biol.*, vol. 419, pp. 108–115, Apr. 2017.
- [29] F. De Vico Fallani, J. Richiardi, M. Chavez, and S. Achard, "Graph analysis of functional brain networks: Practical issues in translational neuroscience," *Phil. Trans. Roy. Soc. B, Biol. Sci.*, vol. 369, no. 1653, Oct. 2014, Art. no. 20130521.
- [30] J.-H. Wang, X.-N. Zuo, S. Gohel, M. P. Milham, B. B. Biswal, and Y. He, "Graph theoretical analysis of functional brain networks: Test-retest evaluation on short- and long-term resting-state functional MRI data," *PLoS ONE*, vol. 6, no. 7, Jul. 2011, Art. no. e21976.
- [31] M. M. Shafi, M. B. Westover, M. D. Fox, and A. Pascual-Leone, "Exploration and modulation of brain network interactions with noninvasive brain stimulation in combination with neuroimaging," *Eur. J. Neurosci.*, vol. 35, no. 6, pp. 805–825, Mar. 2012.
- [32] K. Bansal, J. Nakuci, and S. F. Muldoon, "Personalized brain network models for assessing structure–function relationships," *Current Opinion Neurobiol.*, vol. 52, pp. 42–47, Oct. 2018.
- [33] S. He and J. Song, "Finite-time sliding mode control design for a class of uncertain conic nonlinear systems," *IEEE/CAA J. Automatica Sinica*, vol. 4, no. 4, pp. 809–816, Sep. 2017.
- [34] S. He, Q. Ai, C. Ren, J. Dong, and F. Liu, "Finite-time resilient controller design of a class of uncertain nonlinear systems with time-delays under asynchronous switching," *IEEE Trans. Syst., Man, Cybern. Syst.*, vol. 49, no. 2, pp. 281–286, Feb. 2019.
- [35] X. Lyu, Q. Ai, Z. Yan, S. He, X. Luan, and F. Liu, "Finite-time asynchronous resilient observer design of a class of non-linear switched systems with time-delays and uncertainties," *IET Control Theory Appl.*, vol. 14, no. 7, pp. 952–963, Apr. 2020.
- [36] A. M. Stuart, "Inverse problems: A Bayesian perspective," *Acta Numerica*, vol. 19, p. 451, May 2010.
- [37] K. Ray, "Bayesian inverse problems with non-conjugate priors," *Electron. J. Statist.*, vol. 7, no. none, pp. 2516–2549, Jan. 2013.
- [38] J. Adler and O. Öktem, "Deep Bayesian inversion," 2018, *arXiv:1811.05910*. [Online]. Available: <http://arxiv.org/abs/1811.05910>



**YOUNGJOON HONG** was born in Seoul, South Korea. He received the B.S. degree in mathematics from Korea University and the Ph.D. degree in mathematics from Indiana University, in 2015.

From 2015 to 2018, he was a Research Assistant Professor with the University of Illinois, Chicago. Since 2018, he has been an Assistant Professor with the Department of Mathematics and Statistics, San Diego State University. His research interests include applied analysis and computational mathematics. Much of his works is motivated by connections between practical applications, such as computational fluid dynamics, geophysics, electromagnetism, nonlinear waves, data science, and deep learning.



**BONGSUK KWON** was born in Busan, South Korea. He received the B.S. degree from Korea University, the M.S. degree from the Pohang University of Science and Technology, and the Ph.D. degree from Indiana University, Bloomington, in 2009, all in mathematics.

From 2009 to 2012, he was a Visiting Assistant Professor with the Department of Mathematics, Texas A&M University, College Station. He joined the Ulsan National Institute of Science and Technology, Ulsan, South Korea, in 2012, where he is currently an Associate Professor of mathematics. His main research interest includes theory of partial differential equations arising from continuum mechanics, which include stability and the asymptotic behavior of nonlinear waves.



**BYUNG-JUN YOON** (Senior Member, IEEE) received the B.S.E. degree (*summa cum laude*) from Seoul National University, Seoul, South Korea, in 1998, and the M.S. and Ph.D. degrees from the California Institute of Technology, Pasadena, in 2002 and 2007, respectively, all in electrical engineering. He joined the Department of Electrical and Computer Engineering, Texas A&M University, College Station, in 2008, where he is currently an Associate Professor. He also

holds a joint appointment with the Brookhaven National Laboratory (BNL), Upton, NY, USA, where he is currently a Scientist in Computational Science Initiative (CSI). His main research interests include optimal experimental design, objective uncertainty quantification, and scientific machine learning for a wide range of applications, including bioinformatics, computational network biology, and materials science. His recent honors include the National Science Foundation (NSF) CAREER Award, the Best Paper Award at the Ninth Asia Pacific Bioinformatics Conference (APBC), the Best Paper Award at the 12th Annual MCBIOS Conference, and the SLATE Teaching Excellence Award from the Texas A&M University System.

...